Pediatric Dermatology Vol. 23 No. 5 507–510, 2006

Successful Treatment of Pediatric Psoriasis with Indigo naturalis Composite Ointment

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Abstract: The treatment of psoriasis in children is still an intractable problem and demands a long-term therapy with prolonged efficacy that is free from serious adverse events. Many modes of therapy are currently in use but the disease is often resistant to treatment owing to the unacceptable toxicity that leads to poor compliance. Therefore, to develop an alternative treatment is indispensable. Traditional Chinese medicine has been documented for over 1000 years to provide various effective treatments for inflammatory skin diseases. Herein, we report an 8-year-old boy with recalcitrant pediatric psoriasis who, after multiple treatment failures with conventional antipsoriatic medications, showed remarkable clinical improvement with 8 weeks of topical treatment with Indigo naturalis composite ointment. Remission has lasted for over 2 years until now. Our patient's response suggests that topical Indigo naturalis composite ointment may provide a safe and effective alternative treatment for pediatric psoriasis.

Psoriasis may present in diverse clinical manifestations, from the classical plaque psoriasis, to pustular psoriasis and to explosive guttate psoriasis. Although the onset of psoriasis in the majority of patients is within the third decade, it can occur in childhood, representing one of the papulosquamous diseases that accounts for 10% of all cutaneous disorders commonly seen in a pediatric dermatology clinic (1). The therapy of psoriasis in children should be as conservative as appropriate for the different types and severities, as both effectiveness and long-term safety are important.

Traditional Chinese medicine (TCM) is one of the alternative therapeutic options that has been reported to exhibit a potential antipsoriatic efficacy in the Chinese literature (2). Among these, Indigo naturalis (Qing Dai) has been used for the treatment of psoriasis by systemic therapy (3). However, long-term systemic use was often associated with adverse gastrointestinal effects. To optimize the use of Indigo naturalis as an antipsoriasis medicine, a topical treatment without apparent systemic adverse effects became the first choice. We formulated an ointment with Indigo naturalis, Scutellaria baicalensis-Georgi (Huang Qin) and Cortex phellodendri (Huang Bai), and investigated its use as a topical psoriatic treatment. We reported one child with recalcitrant psoriasis, who showed significant clinical improvement after treatment with this topical Indigo naturalis composite ointment.

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CASE REPORT

The patient was an 8-year-old male child, who had widespread psoriasis of 2 years' duration. He was otherwise healthy except for a past history of allergy rhinitis, whereas his mother had a 30-year history of chronic plaque psoriasis. Initially, at the age of 6 years, he developed red, raised papules on his scalp, which then spread to his trunk. The lesions were first mistakenly diagnosed as eczema and failed to respond to a variety of treatments (steroid and antihistamine) prescribed by a local dermatologist. Factors that exacerbated the lesions included the common cold, stress, shellfish consumption, and spicy or fried foods. He was thereafter referred to a medical center and diagnosed with pediatric psoriasis. Subsequently, he received the conventional therapies including vitamin D3 analogues and phototherapy. Excellent results were produced at the beginning, but symptoms worsened after prolonged treatment.

When he first visited our outpatient clinic, scaly round papules were scattered over his body sparing only his face (Fig. 1). With the consent form signed by his parents and the approval of the institutional review board of our hospital, we applied the Indigo naturalis composite ointment to his psoriatic lesions twice a day and discontinued all other medications. After continuing this treatment for 2 months, the psoriatic lesions on his body disappeared completely (Fig. 2) and the involved total body surface decreased from almost 80% to 0%. No allergic reaction or dermatitis was observed, and the skin lesions continued to be in remission during 1-year follow-up period. Only one to three small papules occasionally flared over his elbows, buttocks, and knees when triggered by upper airway infection, stress, or food sensitivities, but these subsided soon after re-applying the ointment. No significant abnormalities in hematologic examinations, liver, and renal function were found throughout the follow-up period.

Figure 1. Before treatment, the body surface was involved with red, raised macules and papules.

Figure 2. After 2 months of treatment, the psoriatic lesions on the body have vanished and skin has resumed a normal appearance.

DISCUSSION

Psoriasis in childhood is a disease of many forms that may change over time. The most common form is the medium to large plaque type (4,5). Compared with those in adults, the plaques are usually smaller and the scales

are finer and softer in children. The cause of psoriasis appears to be multifactorial, with both genetic and environmental factors playing major roles. A positive family history of psoriasis has been found in up to 71% of pediatric patients (5). Human leukocyte antigen types Cw6 and DR7 are found to link with the early onset of psoriasis (6).

The triggering factors of psoriasis include local injury, infection (especially *Streptococcus*), and medications (e.g., systemic steroids, lithium, antimalarials, and beta-blockers). The treatment objectives in childhood psoriasis are to preserve skin surfaces, to afford physical relief from the disease, and to employ treatments that do not endanger the future healthy development of the child (7). Conventional treatment for psoriasis has several disadvantages, including inconvenience (as is the case with topical therapy and phototherapy) and toxicity (as is the case with PUVA, acitretin, and immunosuppressants), which may lead to poor compliance and result in subsequent flares (8). Therefore, it is important to explore an alternatively new intervention that can prolong the remission duration of psoriasis or prevent progression.

Chinese herbal medicines provide alternative approaches to treat psoriasis. Most of the key actions in these herbal medicines involve anti-inflammatory properties, modulation of cytokine production, or inhibition of angiogenesis. All these actions are potentially relevant in reducing the severity of psoriasis (2).

Instead of oral ingestion, the use of topical application can avoid first-pass effect and chemical degradation of the drug in the gastrointestinal tract, as well as minimizing the risk of toxic side effects including gastric irritation and liver damage. As psoriasis is a persistent and recurring disease, patients often require continuous treatment, preferably with a medication with a low cumulative toxicity potential (9). Topical application should not only result in direct and better therapeutic efficacy but also avoid the long-term adverse reactions.

The topical ointment we used combines three herbs, Indigo naturalis, *Scutellaria baicalensis*-Georgi, and Cortex phellodendri, which are recommended for psoriatic treatment in TCM. These herbs were identified and provided by the Chinese Medicine Pharmacy of our institution. They were finely ground in a hammer mill until they could pass through a 75 μm screen and were mixed in the ratio of 1:2:2 (Indigo naturalis:*Scutellaria baicalensis*-Georgi:Cortex phellodendri). To make the mixed herbs easily applicable, the final ointment was prepared by formulating 20% mixed herbs and 80% vehicle containing 25% vaseline, 30% yellow wax, and 45% olive oil.

Indigo naturalis, the key component of our ointment, is a dark blue powder prepared from the leaves of *Baphicacavthus cusia (Nees) Bremek* that has been used to treat infectious and inflammatory diseases. Indigo naturalis and one of its active ingredients, indirubin, have been reported to be effective in treating chronic granulocytic leukemia and psoriasis (10). Recent pharmacologic studies also showed that both had antiviral, anti-bacterial, and antitumor effects (11,12). However, Indigo naturalis and indirubin both have poor solubility and low absorption, and systemic use had been associated with side effects such as gastrointestinal and liver damage (13). Topical treatment may produce less adverse effects.

Scutellaria baicalensis-Georgi has been used since ancient times to treat allergic and inflammatory disease in China and Japan. Several major flavonoids, including baicalein, baicalin, oroxylin, and wogonin have been isolated from this plant. Baicalein and baicalin, two major flavonoids of *Scutellaria baicalensis*-Georgi, have already been demonstrated to exert antiangiogensis, antiproliferative, anti-inflammatory, antiviral, antithrombotic, antioxidant, and anticancer effects (14,15).

Cortex phellodendri is made of the dried trunk bark of a rutaceous plant. It is known to contain berberine, palmatine, jatrorrhizine, phellodendrine, and magnoflorine. Among these ingredients, berberine has many pharmacologic effects, including the inhibition of DNA and protein synthesis, arresting cell cycle progress, antiproliferative as well as anti-inflammatory, and anticancer effects (16,17).

A skin biopsy was not performed on this child because of ethical considerations. However, the remarkable clinical outcome appeared to be convincing and prompts us to further conduct a thorough clinical trial using the Indigo naturalis composite ointment.

In conclusion, we report a TCM-based therapy that exhibits several advantages in treating pediatric psoriasis. It is effective, safe, and the remission of disease symptoms seems to be long-lasting. In addition, it costs much less in comparison with other topical agents. This report warrants further investigation into the systematic clinical efficacy of this treatment method for psoriasis and a mechanistic study of its drug actions.

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